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PAIN MANAGEMENT IN INTENSIVE CARE UNIT: A BRIEF REVIEW

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ABSTRACT

Pain is a common and major public health problem. It is an unpleasant experience for all patients especially the critical patients in the intensive care unit (ICU), where the majority of the patients are unable to report or express their pain. The adequate pain assessment and management results in a better outcome in ICU patients and if not treated properly, pain can have various acute and chronic adverse effects on the patient's well-being including post-traumatic stress disorder. Various pain assessment tools including behavioral pain scales are used in ICU. Treatment of pain involves the role of a multidisciplinary team using various therapies to make the patient pain free and comfortable. The assessment of various factors like the conscious level of the patient, presence of mechanical ventilator and various invasive catheters, hemodynamic stability, and presence of organ dysfunction plays an important role in determining the therapeutic option to be used for the treatment of pain.

REVIEW ARTICLE

INTRODUCTION

The critical care (intensive care) is a dedicated specialty in healthcare which involves multidisciplinary management of patients with acute and often life-threatening organ dysfunction or disease [1]. The goal of an intensivist is to save the patient's life by preventing any further physiologic worsening/deterioration of the patient by management and treatment of acute and/or severe diseases [1]. The intensive care unit (ICU) provides the required environment and support for these critically ill and mechanically ventilated patients who need a specific physical space, monitoring technology, and specialized human resources [2].

The three most relevant and important concepts to be taken care of in an ICU are a

pain, agitation and delirium [2]. Pain is defined in past and present literature as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage" [3, 4]. Agitation and anxiety are common emotions that occur in patients admitted in ICUs and are many times associated with hypoxemia, hypotension, and/or withdrawal from alcohol and other substances and lead to poor outcomes [3]. Delirium is defined as "acute onset of brain dysfunction which is characterized by disturbance in the level of consciousness and cognition changes (memory deficit, disorientation, language disturbance)" [3].

Why do we care about pain management in ICU?

The article "Pain Management: A Fundamental Human Right," published in 2007, Brenan et al wrote: "Unreasonable failure to treat pain is viewed worldwide as poor medicine, unethical practice, and an abrogation of a fundamental human right" [5]. The American Pain Society proposed "Pain measurement" as the fifth vital sign in addition to other vital signs namely blood pressure, pulse rate, temperature, and respiratory rate [6].

Pain, despite the decades of research, remains a significant problem for critical patients throughout their stay in an ICU. The efficient and adequate pain management in a critically ill patient is a complex process that depends upon a comprehensive and systematic assessment of pain. Various researches have proven that inadequate assessment and management of pain can lead to significant physiological and psychological consequences like post-intensive care syndrome and post-traumatic stress disorder in patients discharged from ICU [7-9]. Pain is an underrated and underestimated patient's worst memory of his/her stay in an ICU, even several years after ICU discharge [10].

The inadequate pain control has been found to be associated with various adverse outcomes as enumerated in Table 1, including prolonged mechanical ventilation, increased rate of nosocomial infection, hemodynamic instability, delirium, and decreased immunity [11, 12].

In patients on a mechanical ventilator, pain contributes to reduced cough and hypoventilation which in turn causes sputum retention and increased atelectasis. These mechanisms are the major contributors to the high rate of ventilator-associated pneumonia (VAP), increased duration of mechanical ventilation and length of ICU stay [13]. Numerous other adverse effects of untreated pain in an ICU patient include self-harm from accidental removal of invasive lines or tubes, increased catecholamine release due to sympathetic activation leading to tachycardia and increased systemic vascular resistance, high cardiac workload leading to oxygen supply-demand mismatch and myocardial ischemia [14].

Table 1. Systemic and physiological responses induced by pain

System	Effect
Cardiovascular	Increase in myocardial oxygen demand
Respiratory	Hyperventilation, ventilator dys-synchrony, atelectasis, decreased residual capacity, hypoxia
Gastrointestinal	Low/abnormal motility
Renal	Activation of the renin-angiotensin-aldosterone (RAA) system
Endocrine	Hormonal imbalance (cortisol and insulin) leading to hypotension, hyperglycemia and increased catabolic state
Hematological	Hypercoagulable state and platelet dysfunction leading to high risk of thromboembolic events and gastrointestinal bleeding

Psychological	Depression, anxiety, psychosis, sleep disturbance, fatigue, and serotonergic imbalance
Immune	Suppressed immunomodulation through cytokine elaboration and leukocyte dysfunction (especially natural killer cells)

Assessment of pain in ICU

The assessment and adequate management of pain is one of the most crucial aspects of providing patient comfort in an ICU. The critical patients are usually unable to self-report their discomfort and pain due to sedative drugs, neuromuscular blockers and intubation, likely leading to its underestimation. The increased pain in the ICU patients is mainly associated with respiratory exercises/therapy, wound care, positioning, mobilization, invasive catheters like venous and arterial catheters, nasogastric and chest tube and tracheal suctioning [15, 16].

While assessing the pain, the healthcare provider should include the various aspects of pain:-location, onset, characteristics, severity, duration, progression, quality, any radiation, any relieving and exacerbating factors, and effects of previous therapies.

The pain assessment tools are mainly classified depending upon whether the patient can communicate or not. In the latter circumstances, the healthcare providers consider patient's behavioral changes/reactions as surrogate markers of pain measurement (as long as their motor function is intact) [17].

The gold standard for pain assessment is the self-reporting of pain, but possible in a conscious oriented patient only. The commonly used pain intensity scales useful in awake and cooperative patients are the Numeric Rating Scale (NRS) and the Visual Analogue Scale (VAS) [18]. In an unconscious patient or the patient who is unable to communicate due to sedation, mechanical ventilation or altered sensorium two pain behavior scales have been recommended to assess pain in an ICU: Behavioral Pain Scale (BPS) [19] and Critical Care Pain Observation Tool (CPOT) [20].

Numerical rating scale (NRS)

Patients are required to rate their pain by writing on a 10-point scale [Figure 1] (0, no pain; and 10, most severe pain).

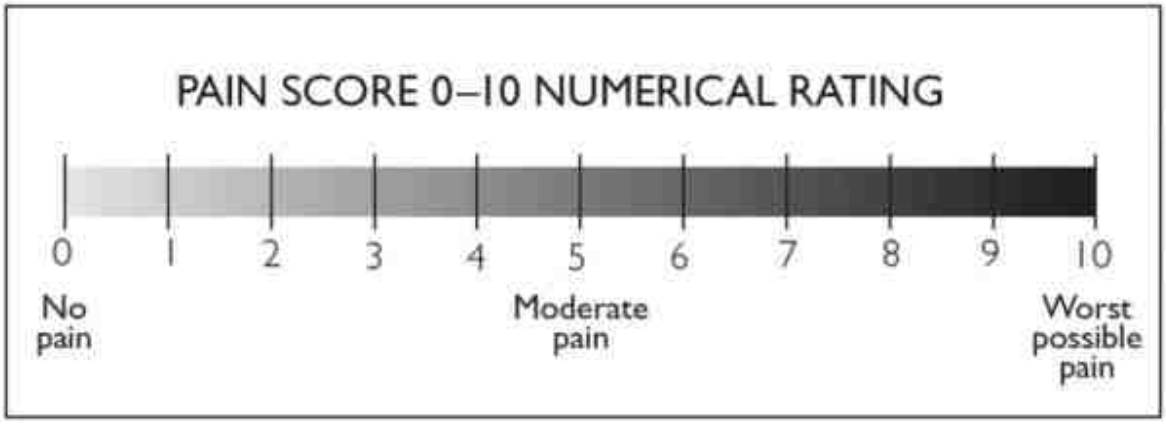

Figure 1: Numerical rating scale (NRS)

Visual analog scale (VAS)

In this assessment, the patients can visualize/see and describe the severity of their pain on a scale of 0–10. Zero for no pain and 10 for maximum pain [Figure 2].

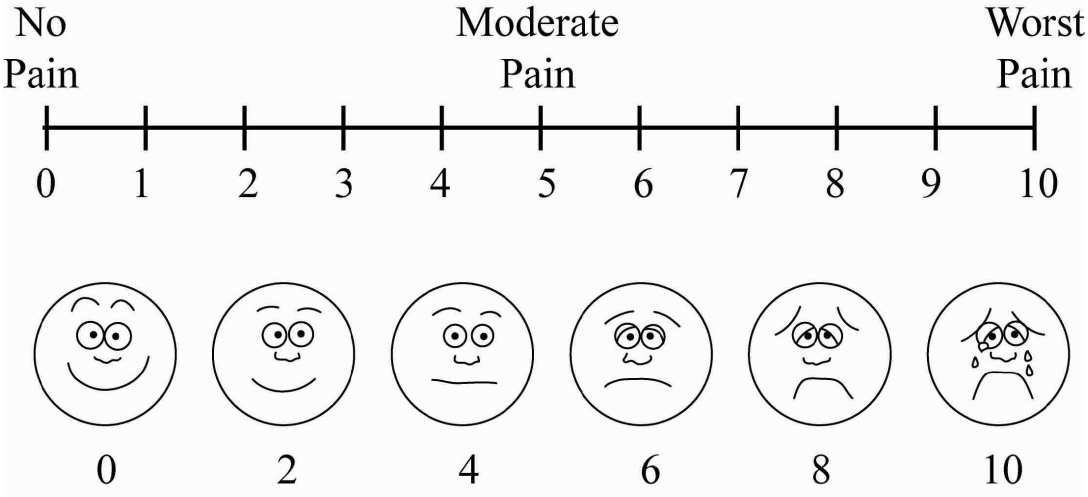

Figure 2: Visual analog scale (VAS)

Behavioral pain scale (BPS)

It is a clinical observational pain score used in patients who are on a ventilator and evaluates three behaviors: facial expressions, upper limb movement/posturing, and ventilator tolerance/compliance [Figure 3]. The BPS score ranges from 3 to 12, and a score of ≥6 describes pain requiring management.

Item	Description	Score
Facial expression	Relaxed	1
	Partially tightened (e.g., brow lowering)	2
	Fully tightened (e.g., eyelid closing)	3
	Grimacing	4
Upper limb	No movement	1
	Partially bent	2
	Fully bent with finger flexion	3
	Permanently retracted	4
Compliance with ventilation	Tolerating movement	1
	Coughing but tolerating ventilation most of the time	2
	Fighting ventilator	3
	Unable to control ventilation	4

Figure 3: Behavioral pain scale (BPS)

Critical care pain observation tool (CPOT)

This pain assessment tool evaluates four clinical components: facial expressions, body movements, muscle tension, and compliance with the ventilator for mechanically ventilated patients or vocalization for the non-intubated patients [Figure 4]. The CPOT score ranges from 2 to 8 and a score of more than 2 require pain management.

Critical Care Pain Observation Tool

Indicator	Description	Score	
Facial expression	No muscular tension observed	Relaxed, neutral	0
	Presence of frowning, brow lowering, orbit tightening, and levator contraction	Tense	1
	All of the above facial movements plus eyelid tightly closed	Grimacing	2
Body movements	Does not move at all (does not necessarily mean absence of pain)	Absence of movements	0
	Slow, cautious movements, touching or rubbing the pain site, seeking attention through movements	Protection	1
	Pulling tube, attempting to sit up, moving limbs/ thrashing, not following commands, striking at staff, trying to climb out of bed	Restlessness	2
Muscle tension Evaluation by passive flexion and extension of upper extremities	No resistance to passive movements	Relaxed	0
	Resistance to passive movements	Tense, rigid	1
	Strong resistance to passive movements, inability to complete them	Very tense or rigid	2
Compliance with the ventilator (intubated patients)	Alarms not activated, easy ventilation	Tolerating ventilator or movement	0
	Alarms stop spontaneously	Coughing but tolerating	1
OR	Asynchrony: blocking ventilation, alarms frequently activated	Fighting ventilator	2
Vocalization (extubated patients)	Talking in normal tone or no sound	Talking in normal tone or no sound	0
	Sighing, moaning	Sighing, moaning	1
	Crying out, sobbing	Crying out, sobbing	2

Figure 4: Critical care pain observation tool (CPOT)

Analgesia administration in ICU patients

The important factor for the pain management in an ICU, when using the pharmacological drugs, is their route or mode of administration. The mode of choice in critically ill patients is the intravenous (IV) administration because the altered gastrointestinal tract function can lead to unpredictable absorption of the enteral medication and the regional hypoperfusion due to shock or subcutaneous edema leads to inadequate absorption of drugs given via the subcutaneous or intramuscular routes.

The factors like the frequency and severity of pain and also the pharmacokinetics of the analgesic medication determine whether the medication to be given as intermittent or continuous infusion administration.

Patient-controlled analgesia (PCA)

It is an effective method for the administration of analgesic medication in an awake and orientated patient and gives the patient a sense of control and autonomy over their pain management.

Nurse-controlled analgesia (NCA)

The nurses administer analgesic medicine as and when required or during the procedures. It is useful but not as superior as the PCA. Regional (nerve blocks) and neuraxial (epidural or spinal) These analgesia techniques are used for selected patients and during surgical procedures. In an ICU patient, the most common regional anesthetic technique used is epidural analgesia. It is quite useful in critically ill postoperative trauma, orthopedic surgery, abdominal, thoracic and major vascular surgery patients.

Common analgesic medications used in ICU Opioids remain the main choice of medications used for giving analgesia in ICU patients due to their high potency along with concomitant sedative and anxiolytic effects. Opioids can be administered via multiple routes. They commonly use opioids include Fentanyl, Remifentanil, and Morphine. The choice of opioid and the dosing should be individualized based on potency, pharmacokinetics and pharmacodynamics, adverse effect, patient comorbidities and organ dysfunction [21]. Table 2 enumerates common analgesics and their pharmacology.

Table 2: Common analgesics and their pharmacology

Analgesic medications	**Dosage**	**Half-life**	**Main adverse effects**
Morphine	2–5 mg bolus, 1–10 mg/hour infusion	2–4 h	Hypotension, metabolites accumulation in renal in impairment
Fentanyl	25–100 µg bolus 25–200 µg/hour	2–5 h	Muscle rigidity, accumulation in hepatic impairment
Remifentanil	0.5–2 mg bolus 0.5–15 µg/kg/hour	3–10 minutes	Bradycardia, hypotension
Dexmedetomidine	0.2–1.4 µg/kg/hour	6 minutes to 3 h	Bradycardia, hypotension
Paracetamol	1 g every 6 h	2–3 h	Liver and kidney injury

Morphine: It is the most frequently used analgesic medication, especially in cancer patients, which is mainly metabolized in the liver and excreted through kidneys. Morphine has active metabolites namely: morphine-3-glucuronide and morphine-6-glucoside, which can accumulate in renal insufficiency and cause opioid toxicity and adverse effects like nausea, sedation, respiratory depression, myoclonus and in some cases seizures. Morphine also stimulates the release of histamine which in turn causes vasodilation leading to cardiovascular instability.

Fentanyl: It is a synthetic opioid that is almost 100 times more potent than morphine. Unlike morphine, it does not stimulate histamine release; therefore it causes no vasodilation or hypotension, making it the preferred drug for hemodynamically unstable patients. It is also more lipid-soluble as compared to morphine and if administered for more than 5 days it accumulates in the fatty tissue and is released from thereafter the drug is stopped leading to prolonged sedation.

` **Remifentanil:** As compared to morphine, it is 200 times more potent and also quick-acting and an equally quick recovery drug.

Tramadol: It is a centrally acting opioid-like medication that acts by binding to the µ-opioid receptors on neurons. It is also a serotonin-norepinephrine reuptake inhibitor (SNRI). The common side effects of tramadol include nausea, vomiting, dizziness, drowsiness, dry mouth and headache.

Non-opioid analgesic agents

Non-opioid analgesics are used in the management of pain either alone or as an adjunct with opioid analgesics. This helps in decreasing the required dose of opioids and thus decreasing the opioid-related side effects.

Nonsteroidal anti-inflammatory drugs (NSAIDs)

NSAIDs administration in ICU patients is controversial although they have an opioid-sparing effect. The most important adverse effects include renal dysfunction,

gastrointestinal bleeding and inhibition of platelet function.

Paracetamol

It is a common drug used for short-term treatment of pain (mild to moderate) and fever. It has a better safety profile as compared with other NSAIDs (does not cause platelet dysfunction, gastritis or renal toxicity) and opioids (no risk of respiratory depression) [21]. Paracetamol may cause transient abnormalities of liver function if given in high doses.

α2-agonists

The two commonly used α2-adrenoceptor agonists that provide both analgesia and sedation are Clonidine and Dexmedetomidine. As compared to Clonidine, Dexmedetomidine has eight times more affinity for α2-receptors. The patients on Dexmedetomidine infusion have been shown to have decreased prevalence and duration of delirium and confusion when compared with the use of midazolam or morphine [21]. The side-effect of both the α2-agonists includes bradycardia and hypotension.

CONCLUSION

The patients in an ICU are at a higher risk of pain (even at rest) but in most cases unable to describe or communicate their pain. If pain is not adequately treated, it leads to various adverse effects and increases the incidence of chronic pain and post-traumatic stress disorders in these patients. In ICU patients, the presence of anxiety, sleep deprivation and also delirium increases their sensitivity to pain. The organ dysfunctions present in these critical patients may decrease the potency of analgesic medicines and increase their toxicity. Pain assessment is the most important and basic factor of inadequate pain management. The various pain scales are used depending on the patient's abilities to communicate and a multimodal approach is used for analgesia and analgosedation.

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